Appendicitis in children: new insights into an old problem

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Summary

The main aim of this thesis is to evaluate the short – and long-term outcome of non-operative treatment strategy for children with simple appendicitis.

Part 1: Current practice

Till date, appendectomy is the gold standard of choice for treating patients (both adults and children) with acute appendicitis. In chapter two, a comprehensive systematic review discusses some key elements regarding appendectomy. Specific attention is given to the role of laparoscopic appendectomy in managing children with acute simple appendicitis. It was concluded that based upon the available literature definitive conclusions regarding the preferred approach are hard to make. To investigate the outcome of appendectomy in children with simple and complex appendicitis, a retrospective analysis was performed in 878 consecutive children over a ten-year time period. (CHAPTER 3) Children were divided according to disease severity (simple and complex appendicitis). In this study, we noted an intra-abdominal abscess rate (IAA) of 2.6% (7/265), superficial site infection (SSI) rate of 3.4% (9/265) and early readmission rate of 3.4% (9/265) for children with simple appendicitis that underwent an open approach. In those who underwent the laparoscopic approach, an IAA rate of 1.8% (6/333), SSI rate of 1.5% (5/333) and early readmission rate of 2.4% (8/333) was noted. There were no statistical differences regarding these outcomes in the children with simple appendicitis. Lastly, the newly published consensus guideline on the diagnosis and management of acute appendicitis of the European Association of Endoscopic Surgery (EAES) is discussed (CHAPTER 4). Statements and recommendations were formulated based upon a systematic review of the current literature by a team of experts and research fellows, following the Delphi method for reaching consensus. These 46 statements and recommendations were then discussed during the EAES conference in Bucharest in June 2015 and during a web survey. Laparoscopic appendectomy as the treatment of choice for acute simple appendicitis in children reached the benchmark of 70% agreement. Non-operative treatment of simple appendicitis in adults is not suggested due to lacking of high quality evidence at that time.

Part 2 Novel insights: Simple versus complex appendicitis

As two types of appendicitis exist, it is key to differentiate these two types of appendicitis based upon clinical symptoms, laboratory and radiological findings in order to select those patients that might benefit from non-operative treatment (i.e. those with simple appendicitis). In chapter 5, a multiple logistic regression analysis was performed on 64 children with simple appendicitis and 66 children with complex appendicitis. Five variables explained 64% of the variance and were put into our scoring system. An optimal cut-off value was established at < 4. This scoring system was subsequently validated in a second cohort. Positive and negative

likelihood ratio of 10 (4.19-23.42) and 0.11 (0.02-0.71) respectively were demonstrated. Based upon these results, it was concluded that this scoring system could be used to exclude complex appendicitis in clinical practice if the score is < 4. Differences between simple and complex appendicitis not only exist in clinical presentation, but also in the composition of the cellular infiltrate in the inflamed appendix. (CHAPTER 6) Histopathological samples from 24 children with complex appendicitis and 23 children with simple appendicitis were analysed, after immune histochemical staining, using Image J software. We found that the cellular infiltrate in children with complex appendicitis contains significantly more MPO+ cells (neutrophils) and significantly fewer CD20+/CD21+ cells (B-lymphocytes) and CD8+ cells (T-lymphocytes) in comparison to children with simple appendicitis. These findings suggest that simple and complex appendicitis are characterised by a unique immune mononuclear cellular infiltrate in the appendix and might reflect a difference in immune response.

Part 3 Novel insights: Treatment options

Short- and long–term results from initial non-operative treatment strategy for acute simple appendicitis in children is discussed. (CHAPTER 7 & 8) Between September 2012 and June 2014, a prospective non-randomised, multicentre cohort study was performed; including children aged 7-17 years old with a radiological confirmed simple appendicitis. Of 44 eligible patients, 25 participated and were treated with non-operative treatment strategy (inclusion rate 57% [95% CI: 42-70%]). Delayed appendectomy was performed in two, while the other 23 were without symptoms at the 8 weeks follow-up. (CHAPTER 7) In October 2015, these 25 children were compared to the 19 patients who did not wanted to participate and thus underwent an immediate appendectomy. Follow-up period in both cohorts was 25 (16-36) and 26 (17-34) months, respectively. The percentage of patients [95%CI] experiencing complications in the non-operative group and the immediate appendectomy group was 12 [95% CI: 4–30]% and 11 [95%CI:3–31]%, respectively. At 25 months, appendectomy was avoided in 19 of the 25 children (76%). (CHAPTER 8) A potential disadvantage of non-operative treatment is the fact that other types of pathology such as a malignancy when no operation and subsequent histological examination can be missed. A retrospective study in 484 children (241 with simple appendicitis, 222 with complex appendicitis en 21 with a noninflamed appendix) showed that the overall occurrence of unexpected finding was 2.1% in the overall group. (CHAPTER 9) In more detail, unexpected findings during histopathological examination were noted in 4/241 (1.6%) patients with simple appendicitis, 2/222 (1.0%) patients with complex appendicitis and 2/21 (9.6%) patients with a noninflamed appendix. Unexpected findings during surgery were noted in two patients with a noninflamed appendix (ovarian torsion and extensive inflammation of the terminal ileum). Of the ten patients with unexpected findings, only 4 required alteration in treatment.

Lastly, the current available evidence regarding the outcome of initial non-operative treatment strategy is discussed in chapter 10. A systematic review of the literature, identified 5 studies performed in children, including 147 children (non-operative treatment) and 173 children (appendectomy) with one year follow-up. Percentage of children experiencing complications ranged from 0–13% versus 0- 17% for non-operative and appendectomy, respectively. Non-operative treatment avoided an appendectomy in 62-81% of the children after one year follow-up. Although the evidence base for initial non-operative treatment of acute uncomplicated appendicitis in children is by far insufficient, it suggests that the percentage of patients experiencing complications in the initial non-operative treatment group is comparable to the appendectomy group. In addition, it may avoid an appendectomy in the large majority of children after one year follow-up.